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Research Article

In Hospital Mortality Related to Cirrhosis of Liver in a Tertiary Care Rural Hospital

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Abstract: The objective of the study was to identify the causes of mortality among the hospitalsed patients with decompensated cirrhosis of liver and to evaluate for the biochemical and hematological parameters that are related to mortality during hospitalization. Total number of cases are 70 and number of controls are 70. Both cases and controls were compared and found to be age and sex matched. . The Mean age of cases is 46.33 years and the mean age of controls is 45.56 years. The Child-Pugh, MELD and MELD Na scores were computed for each patient on admission. Both cases and control groups contained predominantly male patients, 91.4% and 94.3% respectively. The most common cause of liver dysfunction was found to be alcohol related. The most common cause of admission was hepatic encephalopathy in both groups. The other reasons for admission are renal insufficiency, refractory ascites, upper gastrointestinal bleeding. While evaluating for Chlid status in both groups, 11.4 **%** of patients in both groups had Child's A cirrhosis. 48.6% of cases had Child's B cirrhosis while 52.9% of controls had Child's B cirrhosis. 40.0% cases and 35.7% controls had Child's C cirrhosis. The mean MELD and MELD-Na was significantly higher for the cases group compared to the control group i.e 24.47 & 18.4 for MELD and 29.10 & 23.54 for MELD-Na for the cases and controls respectively. The most common causes of death are due to cirrhosis related complications associated with decompensation like hepatic encephalopathy, hepato renal syndrome and upper gastrointestinal bleeding. A small number of patients died due to non cirrhosis related complications most commonly infections. Univariate analysis was performed on all variables. A p value less than 0.05 was considered statistically significant. This analysis revealed that increasing levels of MELD, MELD- Na, serum creatinine, INR, WBC, neutrophilia and duration of disease were significantly associated with increased risk of death. On multivariate forward stepwise logistic regression, an elevated WBC count (p=0.02, OR 1.2) and creatinine (p=0.003, OR 1.2) were the only factors significantly associated with death. In this study, in hospital mortality in cirrhosis is predominantly due to hepatic dysfunction. The most common cause of mortality in decompensated cirrhosis is due to hepatic encephalopathy, hepato renal syndrome and upper gastro intestinal bleeding. Patients who had died also exhibited higher MELD and MELD sodium value levels. Therefore, when patients are admitted with hepatic decompensation, clinical parameter like duration of disease, hematological parameters like leukocyte count and neutrophilia, biochemical parameters like creatinine, SGPT and INR can help predict short term or in hospital mortality along with MELD and MELD sodium. In this study, Child score did not help in predicting short term mortality in hospitalized patients.

Keywords: Cirrhosis of liver, Mortality, MELD, Biochemical and hematological parameters.

INTRODUCTION

Cirrhosis named by Laennec in 1826 means orange or twany in Greek. Many forms of liver injuries are marked by fibrosis. This response to liver injury is potentially reversible. In contrast, cirrhosis is not a reversible process [1, 2]. Cirrhosis is defined by the World Health Organization (WHO) as a diffuse process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules [3]. The progression of liver injury to cirrhosis may occur over weeks to years. Cirrhosis of liver is a major global health problem, and is the leading cause of death in Asia. An objective and reproducible scoring system for the severity of liver disease is important for predicting mortality in patients with cirrhosis in general or with specific complications of cirrhosis [1]. Cirrhosis can be classified as follows: a) alcoholic; b) cryptogenic or post hepatic; c) biliary; d) cardiac; e) metabolic f) inherited and g) drug related. The clinical presentation of cirrhosis is variable depending on the aetiology and whether hepatocellular or portal hypertension predominates [4]. The profile of cirrhosis may vary with different age and ethnic groups, geographical, social and etiological factors.

The extent and severity of hepatic damage and the degree of dysfunction of other organ systems determine the prognosis of patients with liver cirrhosis. Objective assessment of risk estimates for these patients could provide an empirical basis for resource use, monitoring progress early intervention and evaluating the efficacy of new, and often expensive, therapeutic modalities [5].

Once patients with cirrhosis of liver experience decompensation, mortality risk increases. The causes of mortality in decompensated cirrhosis patients are many fold. Both hepatic dysfunction and non hepatic causes have been implicated in causation of death in decompensated cirrhotic patients.

Not all patients admitted with decompensated cirrhosis deteriorate. Many improve with intensive treatment and are discharged. However some patients deteriorate in spite of intensive treatment and die. The short-term prognosis of acutely ill patients with cirrhosis is influenced by the degree of hepatic insufficiency and by dysfunction of extrahepatic organ systems and systemic response to it.

In 1964 Child and Turcotte described a prognostic model for assessment of surgical risk in cirrhotic patients [6]. In 1973, Pugh et al. used a modified version of this classification for patients undergoing surgical transection for oesophageal varices [7]. The modified Child-Pugh prognostic index has been used extensively to risk-stratify patients with cirrhosis and to evaluate efficacy of therapeutic procedures, *e.g*., sclerotherapy, band ligation, transjugular intrahepatic portosystemic shunt, surgical procedures, *etc*. Interobserver variation for subjective criteria, lack of evaluation of cardiac, renal, pulmonary, acid-base, and electrolyte status, and disregard for important associated factors *viz*. age, AIDS, diabetes, sepsis, and GI bleeding limit the predictive accuracy of Child-Pugh system [5].

Child-Pugh score has been the reference for many years for assessing the prognosis of cirrhosis. However, Child-Pugh score has important limitations, making it difficult to categorize patients according to their own disease severity.

The MELD score originally was developed and validated to assess the short-term prognosis of patients with cirrhosis undergoing the transjugular intrahepatic portosystemic shunt (ie, TIPS) procedure [8]. The score consists of three objective, easily obtainable variables: serum International Normalized Ratio (INR), total bilirubin, and creatinine levels [9]. It subsequently has been shown to be a reliable marker of mortality risk in both hospitalized and ambulatory patients with cirrhosis[10]. The score's usefulness appears to be irrespective of underlying disease etiology.

The model for end-stage liver disease (MELD) score, which was originally designed for assessing the prognosis of cirrhotic patients undergoing transjugular intrahepatic portosystemic shunt (TIPS), is a continuous score relying on three objective variables.

However both CTP score and MELD are associated with many limitations. Mainly they are not used in assessing prognosis during hospitalization. Many other biochemical and hematological variables can be associated with mortality and can be predictive.

Assessment of prognosis during hospitalization mortality can have important role in triaging for level of care.

MATERIALS AND METHODS

Decompensated Cirrhotic patients who died during hospital stay at the Department of Gastroenterology and Hepatology of Narayana Medical College hospital, a tertiary hospital, Nellore AP from January 2011 to December 2012 were studied. Patients with decompensated cirrhosis liver who died during admission within the study period were selected as cases. Patients admitted with cirrhosis and its complications and who improved with treatment followed by discharge were selected as controls. Cases and controls are selected in a blinded manner. Data collected included demographics; etiology of cirrhosis; indication for hospital admission; presence or absence of decompensation and portal hypertension; and the corresponding Child Pugh, MELD, and MELD-Na scores. Other hematological and biochemical markers were studied. The diagnosis of cirrhosis was made by clinical evaluation and with help of investigations. The clinical diagnosis of cirrhosis was made by a history of portal hypertension excluding other etiology, impaired liver function tests, impaired clotting parameters, ultrasonographic or computer tomographic criteria. The Child-Pugh, MELD and MELD Na scores were computed for each patient on admission. The MELD score and MELD Na score was calculated according to the original formula proposed by the Mayo clinic group. The principal study outcome was hospital mortality. The cause of death was also determined.

Exclusion criteria

Patients with portal hypertension not due to primary cirrhosis of liver were excluded. Patients with cirrhosis complicated by space occupying lesions suggestive of hepatocellular carcinoma, detected either by ultra sonogram or computerized tomography were not selected for this study.

Statistical Analysis:

Hematological, biochemical, scoring systems and clinical variables were reported as mean ± SD, and group comparisons between cases and controls were carried out using the independent sample t test. Univariate analysis and multiple forward stepwise logistic regressions were used to identify clinical and

biochemical parameters directly correlated with mortality. *p* value less than 0.05 was considered statistically significant.

RESULTS

Table 1: Demographics, etiology, scores and clinical parameters in mean

	Cases	Controls	p Value
Total Number	70	70	--
Gender	M-64 F-6	M-66 F-4	--
Age(mean)	46.33	45.56	0.07
Duration of disease	20.01	12.76	0.001
Etiology			
Alcohol	44	45	
Viral	15	14	
Others	11	11	
Clinical status			
CTP A	8	8	
CTP B	34	38	
CTP C	28	25	
Child status(Score)	7.8	8.9	0.86
MELD(Mean)	24.47	18.40	0.001
MELD Sodium(Na)	29.19	23.54	0.001
Hemoglobin (%mg)	8.963	8.645	0.358
TC (	11662.86	8170.34	0.004
% of neutrophils	75.01	69.99	0.007
Platelet	110200.00	123871.43	0.336
Creatinine (mg/dL)	1.993	1.1093	0.001
Albumin(mean)	2.313	2.346	0.5
Sodium (meq/L)	123.986	128.146	0.076
SGPT (IU/L)	69.36	47.69	0.039
INR	1.859	1.55	0.008

Total numbers of cases are 70. Total numbers of controls are 70. Both cases and controls were compared and found to be age and sex matched. Both cases and control groups contained predominantly male patients, 91.4% and 94.3% respectively (Table 1). The Mean age of cases is 46.33 years and the mean age of controls is 45.56 years. The mean duration of disease in cases was 20.01 months while the mean duration of disease in controls is 12.76 months. The most common cause of liver dysfunction was found to be alcohol related. The number of hepatic and non hepatic complications in both groups was similar and most patients had 2 or more comorbid conditions. The most common cause of admission was hepatic encephalopathy in both groups. The other reasons for admission are renal insufficiency, refractory ascites, upper gastrointestinal bleeding. While evaluating for Chlid status in both groups, 11.4 **%** of patients in both groups had Child's A cirrhosis. 48.6% of cases had Child's B cirrhosis while 52.9% of controls had Child's B cirrhosis. 40.0% cases and 35.7% controls had Child's C cirrhosis. The mean MELD and MELD-Na was significantly higher for the cases group compared to the control group i.e 24.47 & 18.4 for MELD and 29.10 & 23.54 for MELD-Na for the cases and controls respectively. The most common causes of death are due to cirrhosis related complications associated with decompensation like hepatic encephalopathy, hepato-renal syndrome and upper gastrointestinal bleeding. A small number of patients died due to non cirrhosis related complications most commonly infections. Univariate analysis was performed on all variables .A p value less than 0.05 was considered statistically significant. This analysis revealed that increasing levels of MELD, MELD- Na, serum creatinine, INR, WBC, neutrophilia and duration of disease were significantly associated with increased risk of death (Fig. 2). On multivariate forward stepwise logistic regression, an elevated WBC count (p=0.02, OR 1.2)and creatinine (p=0.003, OR 1.2) were the only factors significantly associated with death (Table 2).

Table 2: Study Results –Variables

Complications		
	Cases	**Controls**
Hepatic related(Mean)	2.20	1.90
Non Hepatic Related Mean)	0.17	0.30
Causes of death		
	Number	**Percentage**
Hepatic encephalopathy	28	37.14
Hepatorenal syndrome	21	30
UGI Bleed	13	18.57
Infection	8	11.42
Others	2	2.85

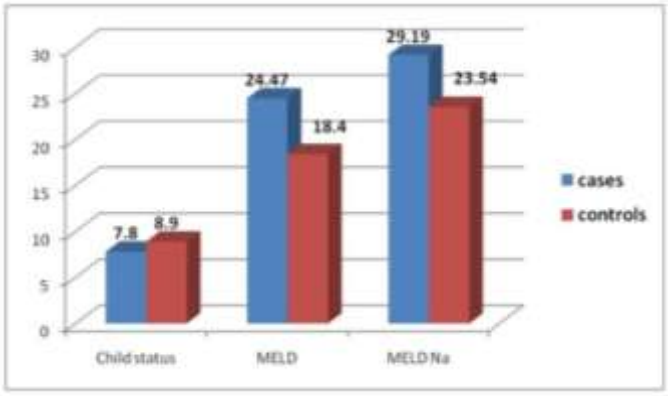

Fig.1: Comparison of Child-Pugh, MELD, MELD Sodium Score

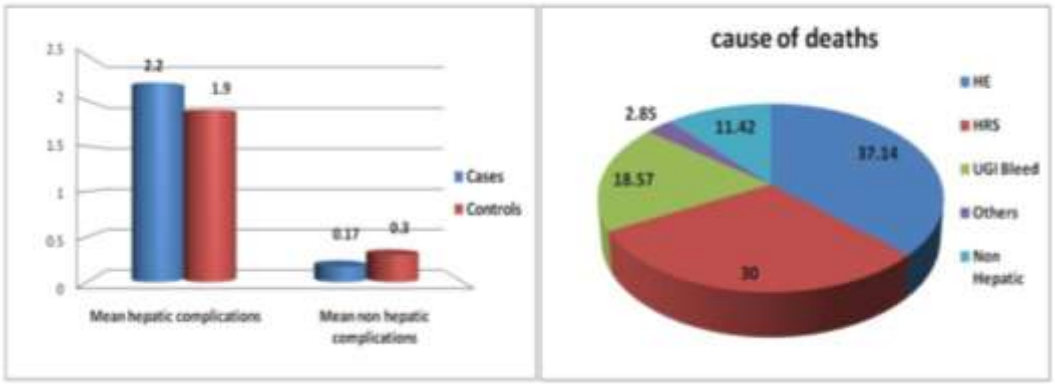

Fig. 2: Complications and causes of death

DISCUSSION

In hospital mortality among cirrhosis of liver patients are due to various factors associated with cirrhosis of liver itself as well as other reasons, but objectively predicting the in hospital mortality at the time of admission is a challenging task as the currently available algorithms and models are not conclusively contributory. Three decades back, the Child-Pugh system is introduced to prognosticate the cirrhotic patients, although, this traditional scoring has several shortcomings as the two important variables in the CTP system have subjective components (encephalopathy and ascities) and so the error possibilities. This issue intensified the search for a continuous disease severity score system that used more objective, readily verifiable parameters, which could be validated as a measure of liver disease severity, or predictor of mortality.

However Child-Pugh score stood the test of time due to its simplicity and easy to calculate at bedside as well, its good accuracy across a broad spectrum of causes and specific situations and so very popular, but the need for more specific and sensitive systems to predict the mortality, especially for the patients undergoing therapeutic procedures led to the development of other models for the same. MELD score comprises only objective variables of serum bilirubin, serum creatinine and INR emerged as a "modern" alternative to Child-Pugh score. Even though MELD is more objective and gives a range for score up to 40, there is no clear evidence that MELD is superior to Child-Pugh score in terms of accuracy. Studies comparing these scores have shown that the accuracy of Child-Pugh score for predicting 3-month to 3-year survival is not always inferior to that of MELD score [4]. In addition, for

many physicians, Child-Pugh score remains more convenient to use at the bedside and more explicit than MELD score.

MELD scoring system found individually to be superior over Child-Pugh in some reports.

In this study, we have evaluated the in hospital mortality association of the 2 scoring systems – CHILD and MELD along with MELD sodium and also various clinical, hematological and biochemical parameters. MELD score has several strengths compared with Child-Pugh. The variables incorporated into the MELD score are simple and more objective. The weight of each variable has been determined by statistical analysis. MELD is a continuous score, which makes it more convenient for scoring individuals within large populations. In addition to organ allocation, MELD score has been validated across a large spectrum of causes of liver diseases. All these reasons make the MELD score likely to be the core tool for assessing the prognosis of cirrhosis in the future. By using MELD score, it can be reasonably assumed that physicians will get landmarks as simple as those they had with Child-Pugh score.

However, as indicated above, the outcome of cirrhosis is quite variable from patient to patient according to different causes, different stages, and different therapeutic options. In parallel, with the expansion of MELD score, several "MELD exceptions" emerged. Therefore, the quest for a universal, simple, and objective scoring system for cirrhosis is likely to remain unsuccessful. Many different scores are available for addressing general or more specific issues regarding the prognosis of cirrhosis. The Child- Pugh score uses two very subjective variables in its calculation- portosystemic encephalopathy and ascites. MELD uses objective variables in their computation. MELD uses prothrombin time INR, serum bilirubin, and serum creatinine levels. In addition to these variables, MELD sodium uses sodium levels for computation

Bacterial infections are a frequent and severe complication of cirrhosis. Cirrhotic patients have an acquired immune deficiency because of dyshomeostasis and malnutrition. All host defense systems are compromised. Moreover, the result of the multivariate logistic analysis showed that an elevated WBC count was associated with in-hospital mortality.

On univariare analysis, mean duration of disease was the demographic which was found to significantly correlate with in hospital mortality. Child score was not found to correlate with in hospital mortality, but both MELD and MELD Na were found to correlate significantly with in hospital mortality. Though hyponatremia was found in previous studies to correlate with early 3 month mortality, it was not significantly correlated with in hospital mortality. This analysis also revealed that increasing levels of serum creatinine, INR, WBC and neutrophilia were significantly associated with increased risk of death. The present study is limited by the omission of the arterial blood gas examination as a result of logistics. Presence of ABG would have facilitated calculating APACHE score. A previous studies by Wehler *et al*. [11] to assess and compare the prognostic accuracy of the Child-Pugh classification, the Acute Physiology and Chronic Health Evaluation (APACHE) II system and the Sequential Organ Failure Assessment (SOFA) for predicting hospital mortality showed that the discriminatory power of the SOFA to predict short-term mortality in critically ill patients with cirrhosis is superior to the APACHE II and Child-Pugh systems. Also Prognostic scoring systems cannot replace the clinical evaluation of the patient.

The present study also confirms that Child score is not predictive of short term mortality. Features of multiple organ involvement like raised renal parameters, coagulopathy and leukocytosis are associated with early or in hospital mortality in comparison to previous study by Wehler *et al*. [11].

In a similar study, comparing in hospital prognosis among cirrhotic patients: Child-Pugh versus APACHE III versus MELD scoring systems concluded that the APACHE III scoring system is superior to Child-Pugh and MELD scoring systems for prognosticating in-hospital mortality among decompensated cirrhotic patients. [12] In the present study, as ABG could not be performed for all patients, APACHE could not be assessed. However components of the APACHE score like creatinine and leukocytosis showed relation to in hospital mortality. The limitations of this present study are the small sample size and lack of follow up of the control group.

CONCLUSION

In this study, in hospital mortality in cirrhosis is predominantly due to hepatic dysfunction. The most common cause of mortality in decompensated cirrhosis is due to hepatic encephalopathy, hepato renal syndrome and upper gastro intestinal bleeding. In this study -Intercurrent infections are associated with mortality and is the most common cause of mortality not related to hepatic decompensation in cirrhotic patients In this study, Longer duration of disease, high leukocyte count, high neutrophilia, higher INR, high creatinine, high SGPT is associated with mortality. Patients who had died also exhibited higher MELD and MELD sodium value levels. Therefore when patients are admitted with hepatic decompensation, clinical parameter like duration of disease, hematological parameters like leukocyte count and neutrophilia, biochemical parameters like creatinine, SGPT and INR can help predict short term or in hospital mortality along with MELD and MELD sodium. In this study -

Child score did not help in predicting short term mortality in hospitalized patients.

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